

CLAIM OR CLAIMS

I/WE CLAIM:

*2nd B3*

1. A mutant ribonuclease inhibitor having at least one amino acid substitution in at least one of its adjacent 5 cysteine residues to an amino acid residue not capable of forming a disulfide bond, the mutant ribonuclease inhibitor having a greater resistance to oxidation, the mutant ribonuclease inhibitor retaining its specificity and binding affinity to ribonuclease.
- 10 2. The ribonuclease inhibitor of claim 1, wherein ribonuclease inhibitor is a human ribonuclease inhibitor and the substituted cysteine residue is in at least one of positions 94, 95, 328 and 329.
- 15 3. The ribonuclease inhibitor of claim 1, wherein the cysteine residue is replaced with an alanine residue.
4. The ribonuclease inhibitor of claim 1, wherein the substitution in at least one of the cysteine residues inhibits the formation of a disulfide bond with an adjacent cysteine residue.
- 20 5. The ribonuclease inhibitor of claim 1, wherein the mutant ribonuclease inhibitor is 10 to 15 fold more resistant to oxidative damage than the native human ribonuclease inhibitor.
- 25 6. The ribonuclease inhibitor of claim 1, wherein the ribonuclease is of the RNASE A superfamily.
7. The ribonuclease inhibitor of claim 1, wherein the modified ribonuclease inhibitor exhibits an *in vitro* inhibition of ribonucleolytic activity.

8. The ribonuclease inhibitor of claim 1, wherein the mutant ribonuclease inhibitor is derived from the native human ribonuclease inhibitor.

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9. A mutant human ribonuclease inhibitor having at least one amino acid substitution in at least one of its adjacent cysteine residues, the substitution being an amino acid other than cysteine, the mutant ribonuclease inhibitor having a greater resistance to oxidation, the mutant ribonuclease inhibitor retaining the specificity and binding affinity to angiogenin of the wild-type human ribonuclease inhibitor.

10. The ribonuclease inhibitor of claim 9, wherein the substituted cysteine residue is in at least one of positions 94, 95, 328 and 329.

11. A DNA sequence comprising a coding sequence encoding a mutant ribonuclease inhibitor which differs from the corresponding wild-type ribonuclease inhibitor in that at least one codon for cysteine has been replaced by a codon for another amino acid.

12. A DNA sequence as claimed in claim 11 wherein the replaced cysteine residue is adjacent to another cysteine residue in the wild-type sequence.

13. A DNA sequence as claimed in claim 11 wherein the ribonuclease inhibitor is human ribonuclease inhibitor and the cysteine replaced is at least one of amino acid positions 94, 95, 328 and 329.

14. A DNA sequence as claimed in claim 11 wherein the substitution is a codon for alanine.

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